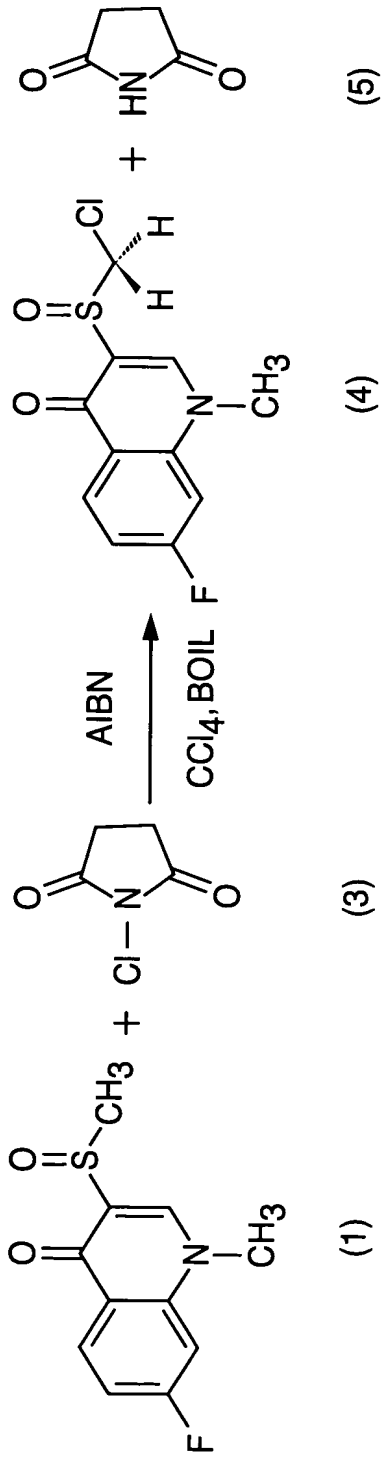

FIG. 1

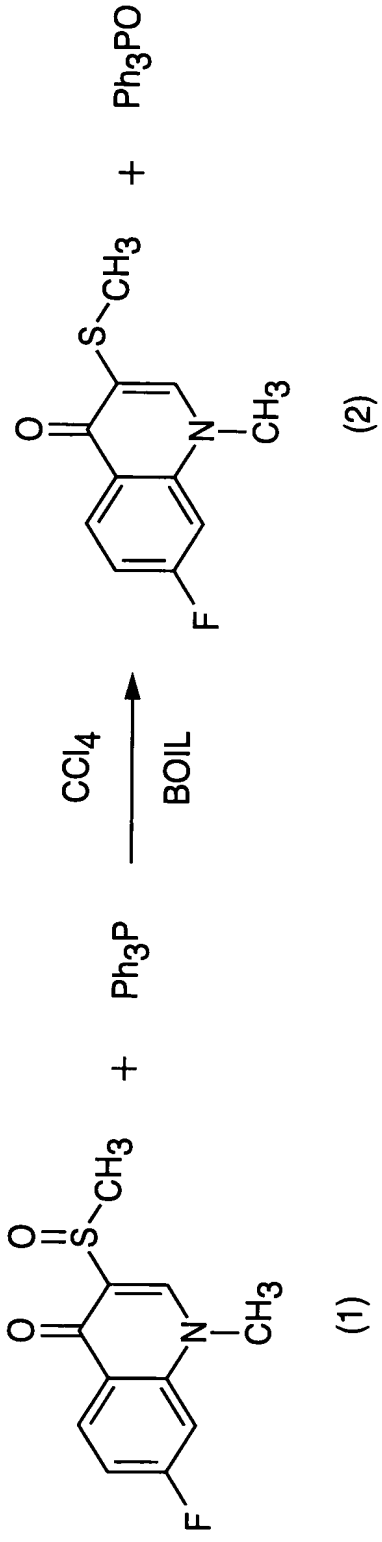

FIG. 2

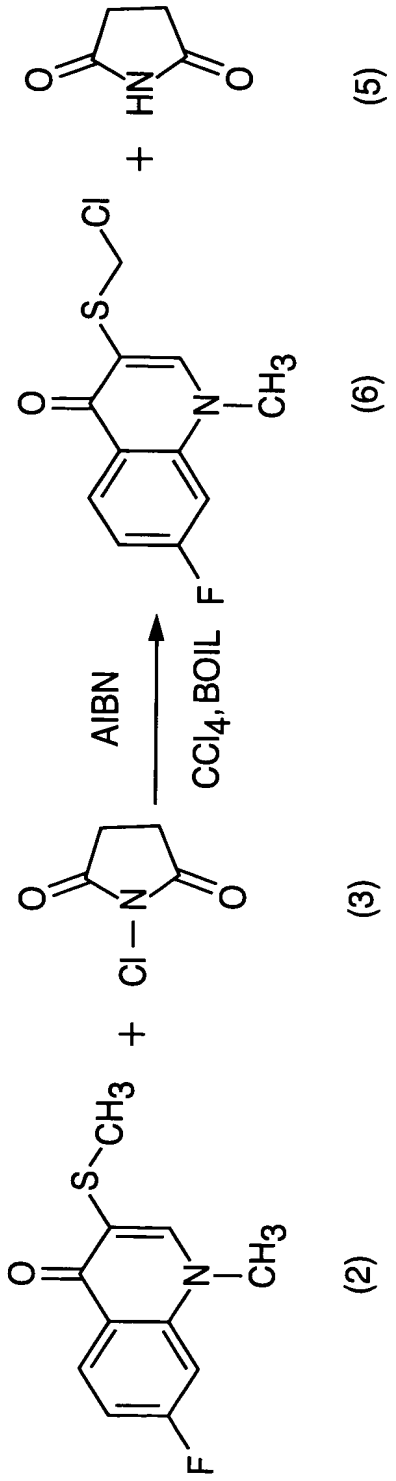

FIG. 3

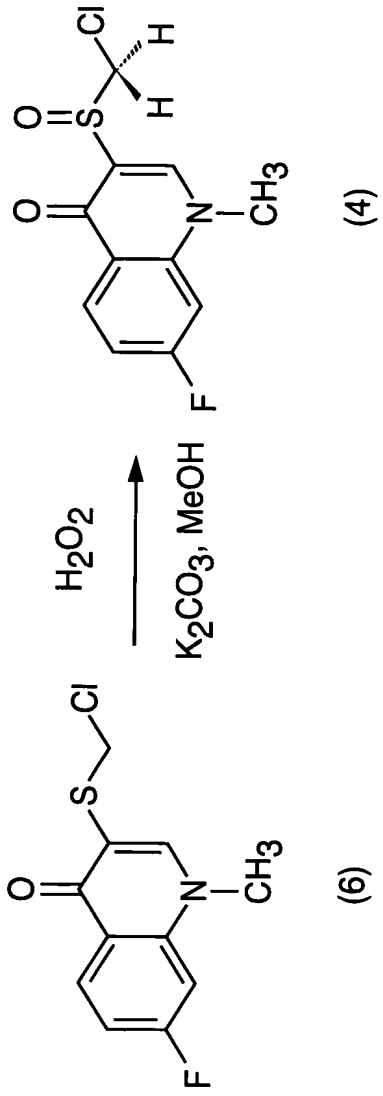

FIG. 4

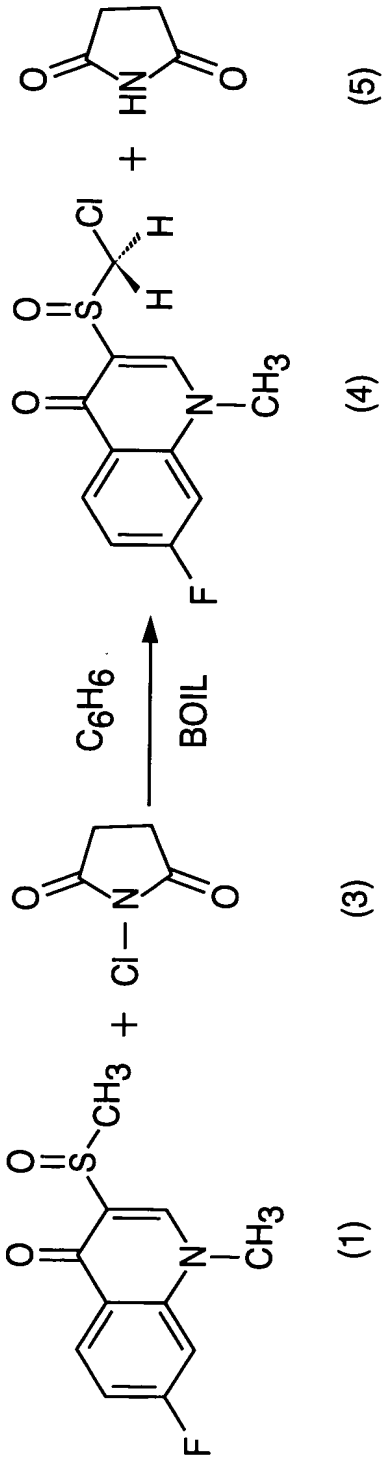

FIG. 5

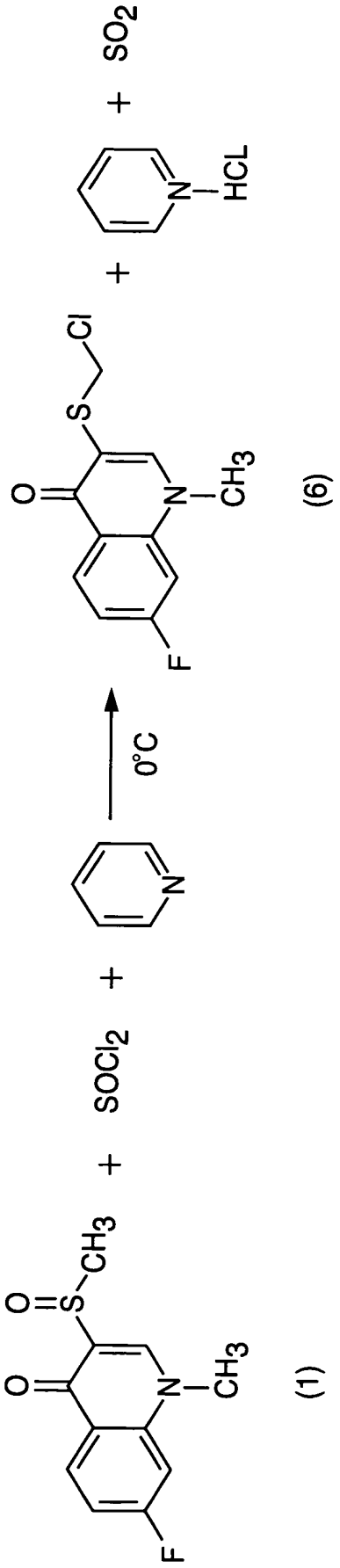

FIG. 6

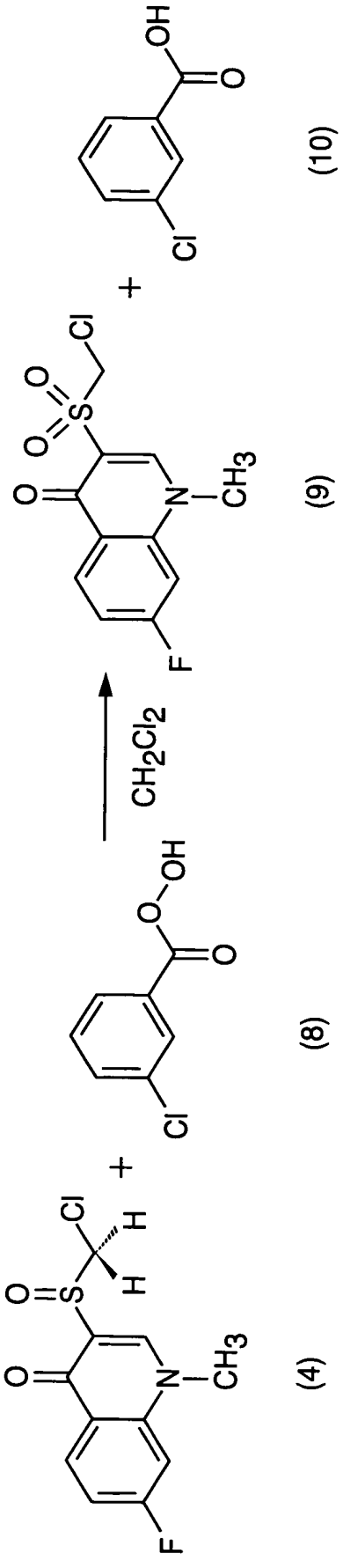

FIG. 7

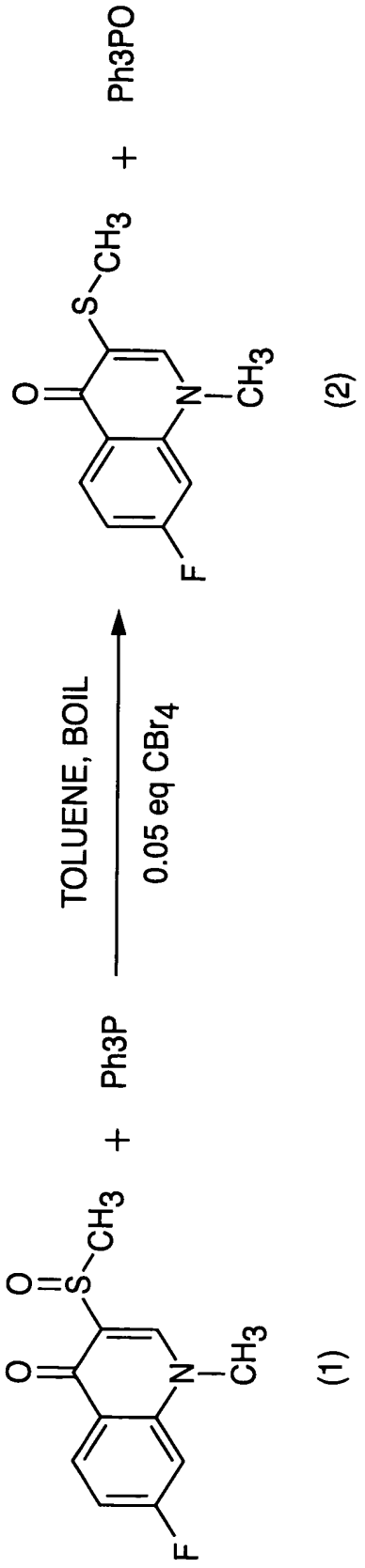
Ph3PO
+
CH3
S
O
N
CH3
F
(2)
TOLUENE, BOIL
0.05 eq CBr4
Ph3P
+
O
O
S
CH3
N
CH3
F
(1)

FIG. 8

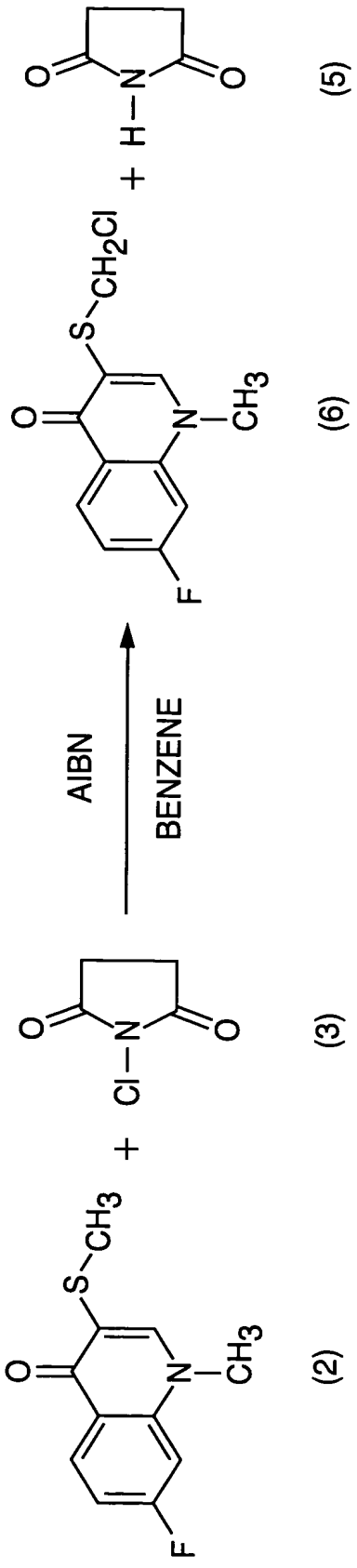

FIG. 9

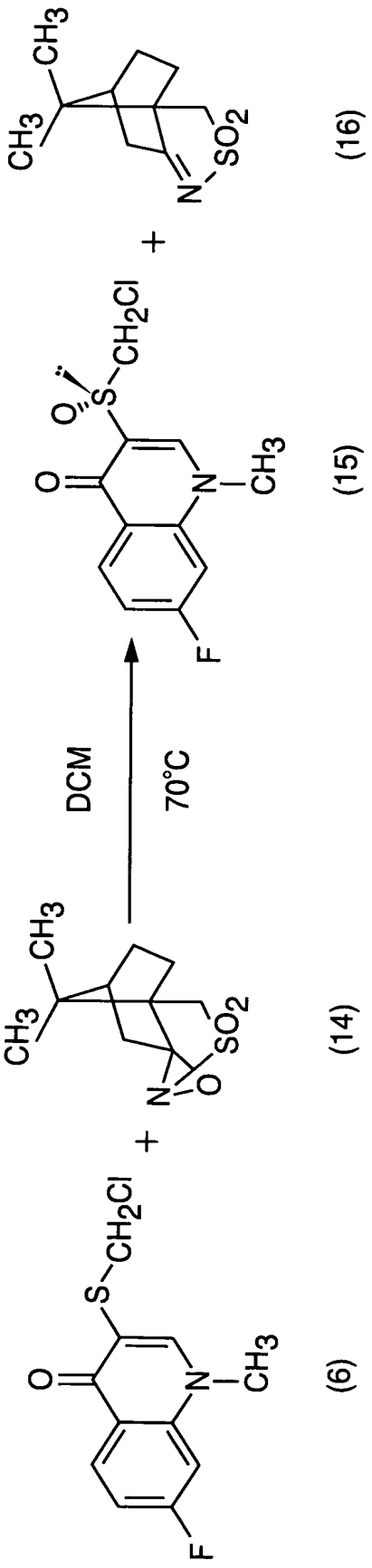
CH3
CH3
SO2
N
(16)
+
CH2Cl
O
S
O
N
CH3
(15)
F
DCM
70°C
CH3
CH3
SO2
O
N
(14)
+
CH2Cl
S
O
N
CH3
(6)
F

FIG. 10

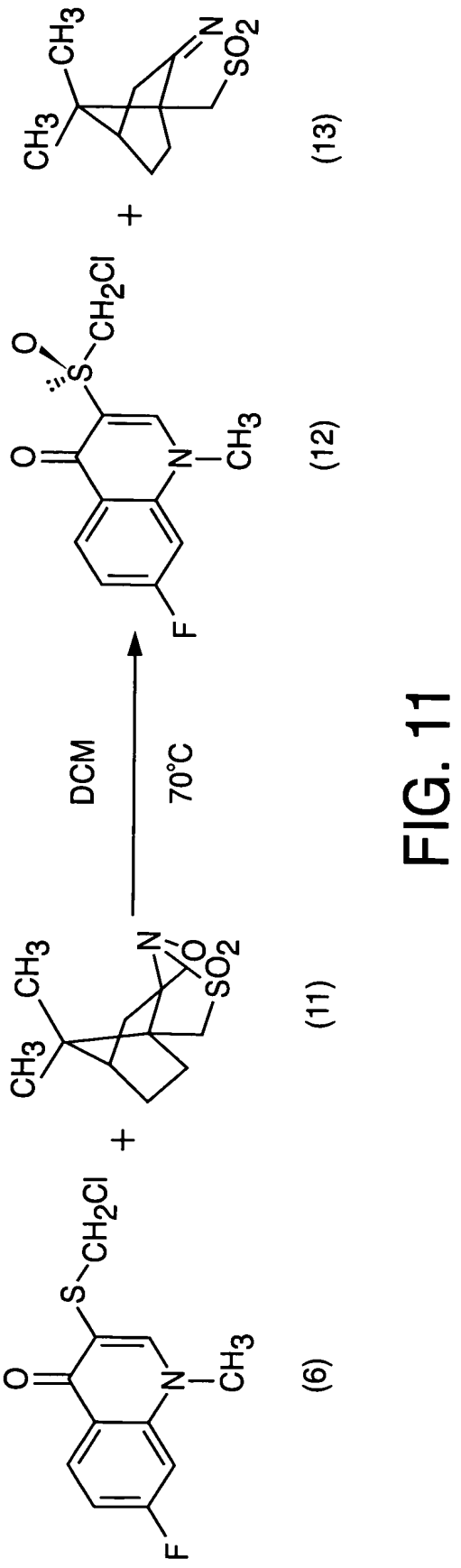
CH3
CH3
N
SO2
(13)
+
O
S
CH2Cl
O
N
CH3
F
(12)
DCM
70°C
CH3
CH3
N
O
SO2
(11)
+
S
CH2Cl
O
N
CH3
F
(6)

FIG. 11

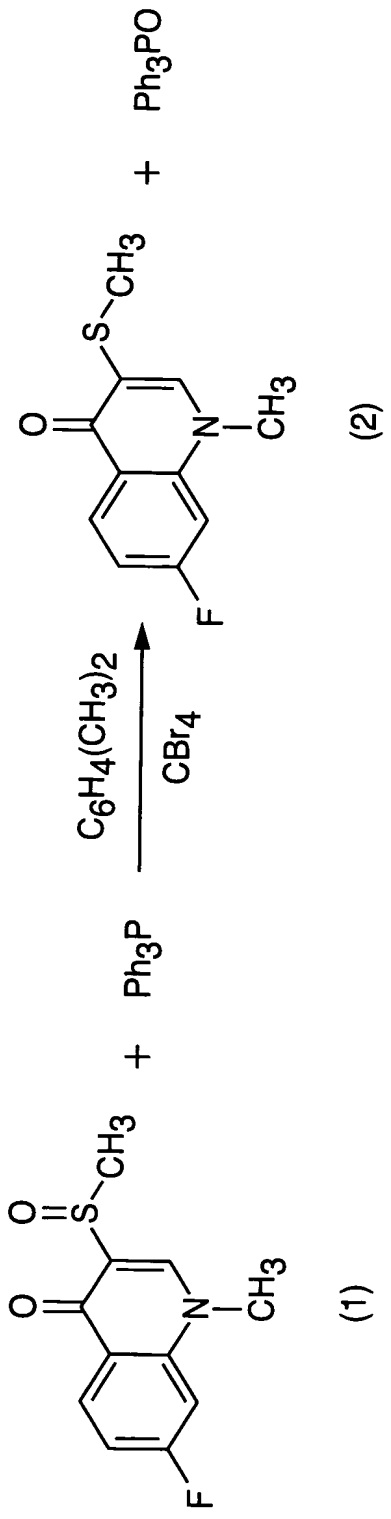

FIG. 12

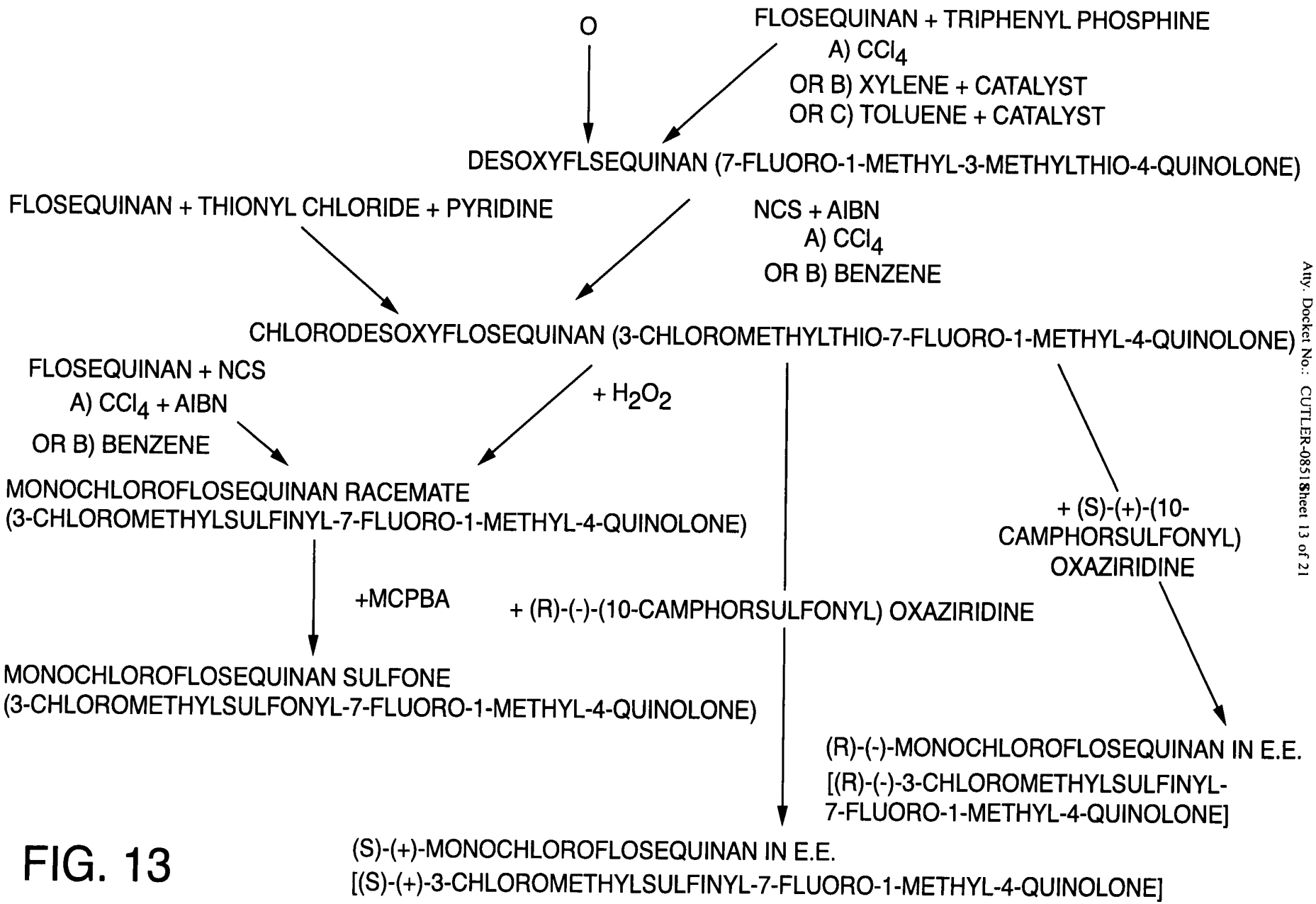

FIG. 13

Continuation of Applin.: 10/281,684
Filed: 10/28/02
Applicant: Stefan Kwiatkowski *et al.*
Title: **Chlorinated Heterocyclic Compounds And Methods Of Synthesis**
Atty. Docket No.: CUTLER-0851 Sheet 13 of 21

CAT. #	TARGET	BATCH*	SPP.	n=	CONC.	†% INHIBITION -100 -50 0 50 100 %	IC_{50}	K_1	n_H	R
146000	PHOSPHODIESTERASE PDE1	41121	BOV	2	100 µM	27				
148000	PHOSPHODIESTERASE PDE2	41120	HUM	2	100 µM	29				
◆152000	PHOSPHODIESTERASE PDE3	41119	HUM	2	100 µM	69				
◆		41564	HUM	2	300 µM	68	95.9 µM			
◆				2	100 µM	51				
				2	30 µM	33				
				2	10 µM	12				
				2	3 µM	6				
				2	1 µM	-1				
154000	PHOSPHODIESTERASE PDE4	41118	HUM	2	100 µM	17				
156000	PHOSPHODIESTERASE PDE5	41117	HUM	2	100 µM	35				
156100	PHOSPHODIESTERASE PDE6	41116	BOV	2	100 µM	17				

Continuation of Appln.: 10/281,684
Filed: 10/28/02
Applicant: Stefan Kwiatkowski *et al.*
Title: **Chlorinated Heterocyclic Compounds And Methods Of Synthesis**
Atty. Docket No.: CUTLER-08518Sheet 14 of 21

*BATCH: REPRESENTS COMPOUNDS TESTED CONCURRENTLY IN THE SAME ASSAY(S).

◆ DENOTES ITEM MEETING CRITERIA FOR SIGNIFICANCE

† RESULTS WITH ≥ 50% STIMULATION OR INHIBITION ARE BOLDFACED
(NEGATIVE VALUES CORRESPOND TO STIMULATION OF BINDING OR ENZYME ACTIVITY)

R=ADDITIONAL COMMENTS

BOV=BOVINE: HUM=HUMAN

FIG. 14

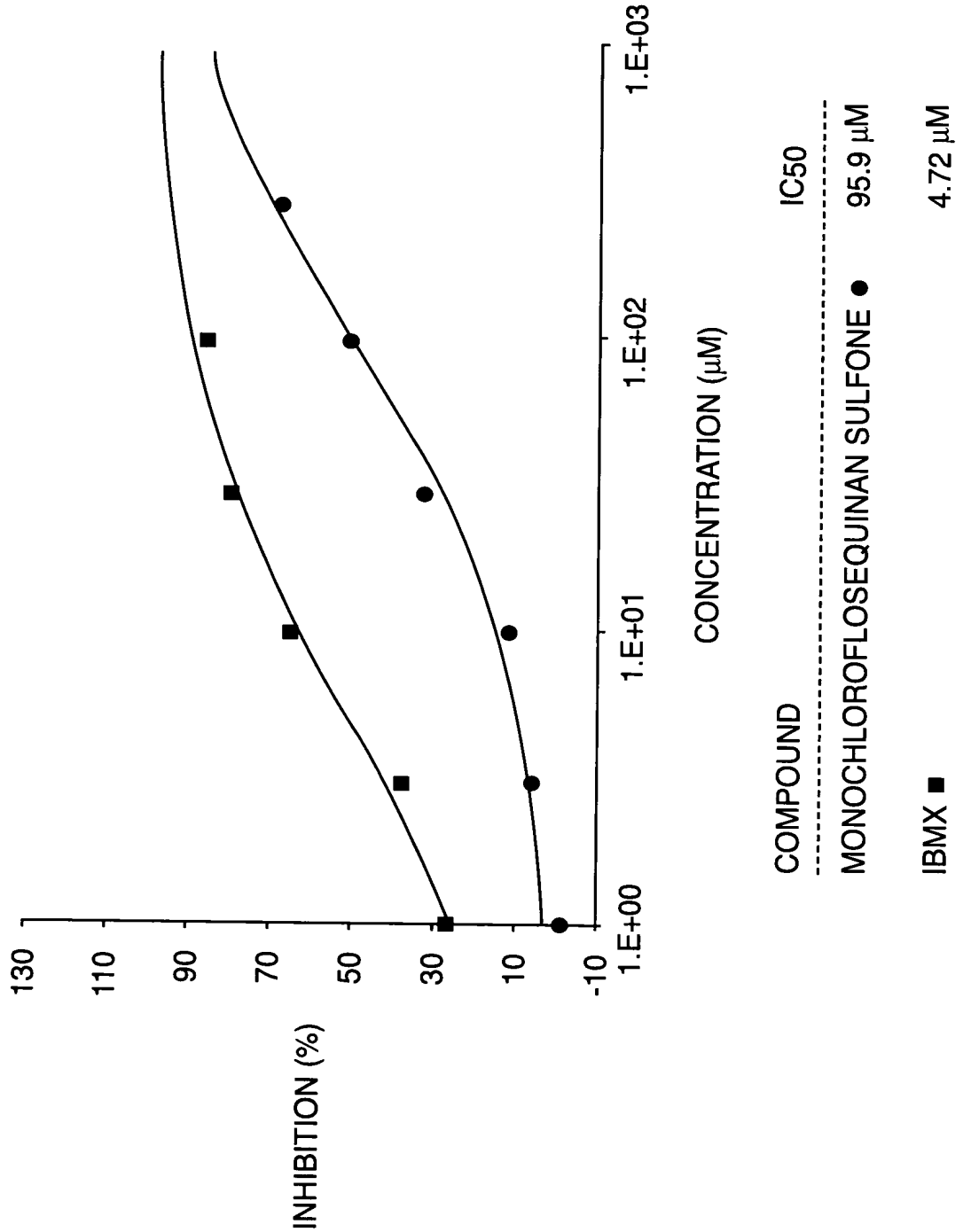
INHIBITION (%)
130
110
90
70
50
30
10
-10
1.E+00
1.E+01
1.E+02
1.E+03
CONCENTRATION (μM)
COMPOUND
IC50
MONOCHLOROFLOSEQUINAN SULFONE ●
95.9 μM
IBMX ■
4.72 μM

FIG. 15

CAT. #	TARGET	BATCH*	SPP.	n=	CONC.	% INHIBITION	IC_{50}	K_1	n_H	R
						-100 -50 0 50 100 %				
◆146000	PHOSPHODIESTERASE PDE1	37070	BOV	2	100 µM	71				
◆		37525	BOV	2	300 µM	65				
◆152000	PHOSPHODIESTERASE PDE3			2	100 µM	55				
				2	30 µM	42	65.6 µM			
				2	10 µM	30				
				2	3 µM	20				
				2	1 µM	19				
◆148000	PHOSPHODIESTERASE PDE2	36815	HUM	2	100 µM	50				
		37526	HUM	2	300 µM	34	>300 µM			
				2	100 µM	20				
				2	30 µM	21				
				2	10 µM	4				
				2	3 µM	2				
				2	1 µM	-3				

FIG. 16A

Continuation of Appln.: 10/281,684
Filed: 10/28/02
Applicant: Stefan Kwiatkowski *et al.*
Title: **Chlorinated Heterocyclic Compounds And Methods Of Synthesis**
Atty. Docket No.: CUTLER-0851 Sheet 16 of 21

CAT. #	TARGET	BATCH*	SPP.	n=	CONC.	†% INHIBITION -100 -50 0 50 100 %	IC_{50}	K_1	n_H	R
◆152000	PHOSPHODIESTERASE PDE3	37072	HUM	2	100 µM	67				
◆		37527	HUM	2	300 µM	73	28.2 µM			
◆				2	100 µM	65				
◆				2	30 µM	58				
				2	10 µM	42				
				2	3 µM	18				
				2	1 µM	1				
154000	PHOSPHODIESTERASE PDE4	36817	HUM	2	100 µM	15				
156000	PHOSPHODIESTERASE PDE5	36818	HUM	2	100 µM	37				
156100	PHOSPHODIESTERASE PDE6	36819	BOV	2	100 µM	16				

*BATCH: REPRESENTS COMPOUNDS TESTED CONCURRENTLY IN THE SAME ASSAY(S).

◆ DENOTES ITEM MEETING CRITERIA FOR SIGNIFICANCE

† RESULTS WITH ≥ 50% STIMULATION OR INHIBITION ARE BOLDFACED
(NEGATIVE VALUES CORRESPOND TO STIMULATION OF BINDING OR ENZYME ACTIVITY)

R=ADDITIONAL COMMENTS

BOV=BOVINE: HUM=HUMAN

FIG. 16B

Continuation of Appln.: 10/281,684
Filed: 10/28/02
Applicant: Stefan Kwiatkowski *et al.*
Title: **Chlorinated Heterocyclic Compounds And Methods Of Synthesis**
Atty. Docket No.: CUTLER-08518Sheet 17 of 21

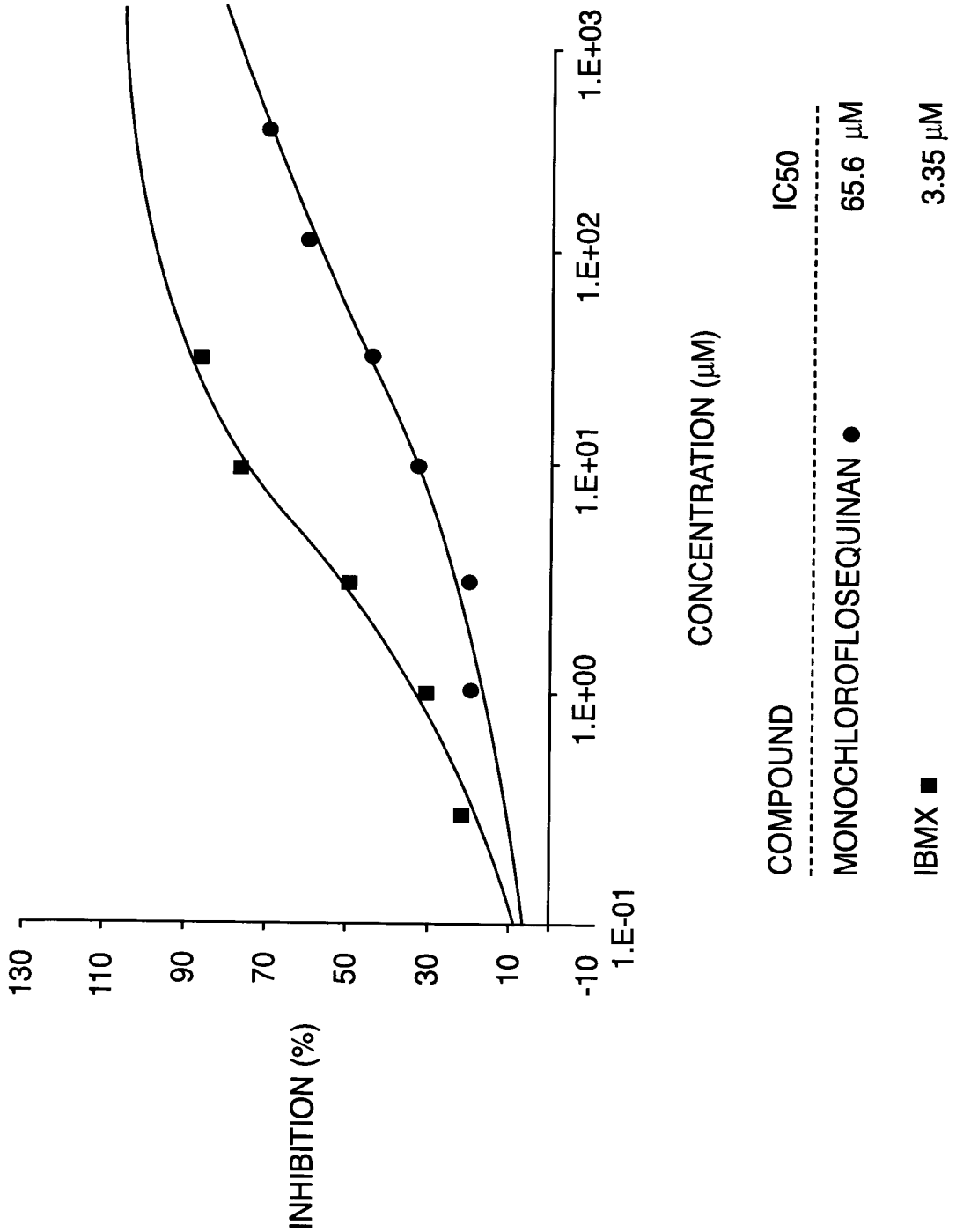
INHIBITION (%)
130
110
90
70
50
30
10
-10
1.E-01
1.E+00
1.E+01
1.E+02
1.E+03
CONCENTRATION (μM)
COMPOUND
IC50
MONOCHLOROFLOSEQUINAN ●
65.6 μM
IBMX ■
3.35 μM

FIG. 17

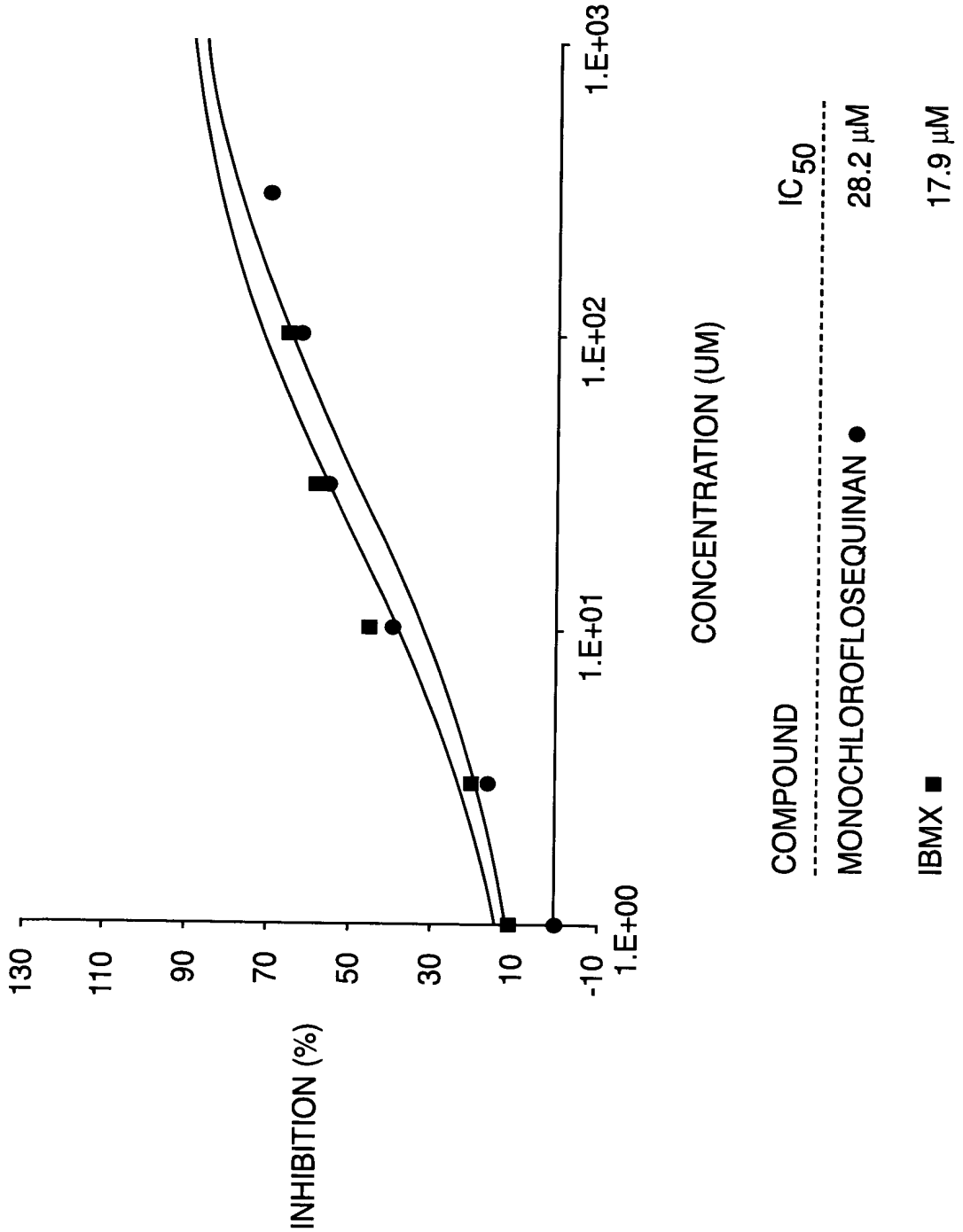
INHIBITION (%)
130
110
90
70
50
30
10
-10
1.E+00
1.E+01
1.E+02
1.E+03
CONCENTRATION (UM)
COMPOUND
IC50
MONOCHLOROFLOSEQUINAN ●
28.2 µM
IBMX ■
17.9 µM

FIG. 18

CAT. #	TARGET	BATCH*	SPP.	n=	CONC.	% INHIBITION -100 -50 0 50 100 %
◆ 146000	PHOSPHODIESTERASE PDE1	49417	BOV	2	200 µM	52
148000	PHOSPHODIESTERASE PDE2	49416	HUM	2	200 µM	41
◆ 152000	PHOSPHODIESTERASE PDE3	49415	HUM	2	200 µM	58
◆ 154000	PHOSPHODIESTERASE PDE4	49414	HUM	2	200 µM	62
156000	PHOSPHODIESTERASE PDE5	49413	HUM	2	200 µM	19
◆ 156100	PHOSPHODIESTERASE PDE6	49412	BOV	2	200 µM	65

FIG. 19

CAT. #	TARGET	BATCH*	SPP.	n=	CONC.	†% INHIBITION -100 -50 0 50 100 %
◆ 146000	PHOSPHODIESTERASE PDE1	49417	BOV	2	200 µM	66
◆ 148000	PHOSPHODIESTERASE PDE2	49416	HUM	2	200 µM	53
◆ 152000	PHOSPHODIESTERASE PDE3	49415	HUM	2	200 µM	86
154000	PHOSPHODIESTERASE PDE4	49414	HUM	2	200 µM	30
◆ 156000	PHOSPHODIESTERASE PDE5	49413	HUM	2	200 µM	51
◆ 156100	PHOSPHODIESTERASE PDE6	49412	BOV	2	200 µM	68

FIG. 20